HeartWare Q&A Slides Shown

April 25, 2012

CSDP

Description of CEC

- CEC comprised of
  - 1 Chairman
  - 2 Reviewers / Review Teams
- Each event goes to the 2 Reviewers or a member of each Review Team
  - If they agree the adjudication is complete
  - If they disagree the Chairman reviews the case and completes the adjudication

CEC Change

- CEC changed during the period of time to the primary endpoint
  - July 26 2010
    - Chair and one CEC member changed
  - August 23 2010
    - 5 CEC members added to Review Teams to assist with backlog
- Subsequently on October 31 2011 the CEC reverted back to 1 Chairman and 2 Reviewers

Changes in Adjudication Event Confirmation

- Good concurrence on assessment of events
- CEC agreed in 97% of adjudications (590/607) that events met the definition of the event as described in the protocol
  - In only 3% (17) cases they did not believe the event met the protocol definition

Heterogeneous Screening

- A two step consenting process was not in place to specifically define screened and enrolled patients
- Standard of care assessments for screening was at Investigators discretion
- Sites likely knew BTT patients lasting status with regards to eligibility – the most common screen failure reason
- Sites had their own screening procedures

Follow-up on 17 Screen Failures with Consent

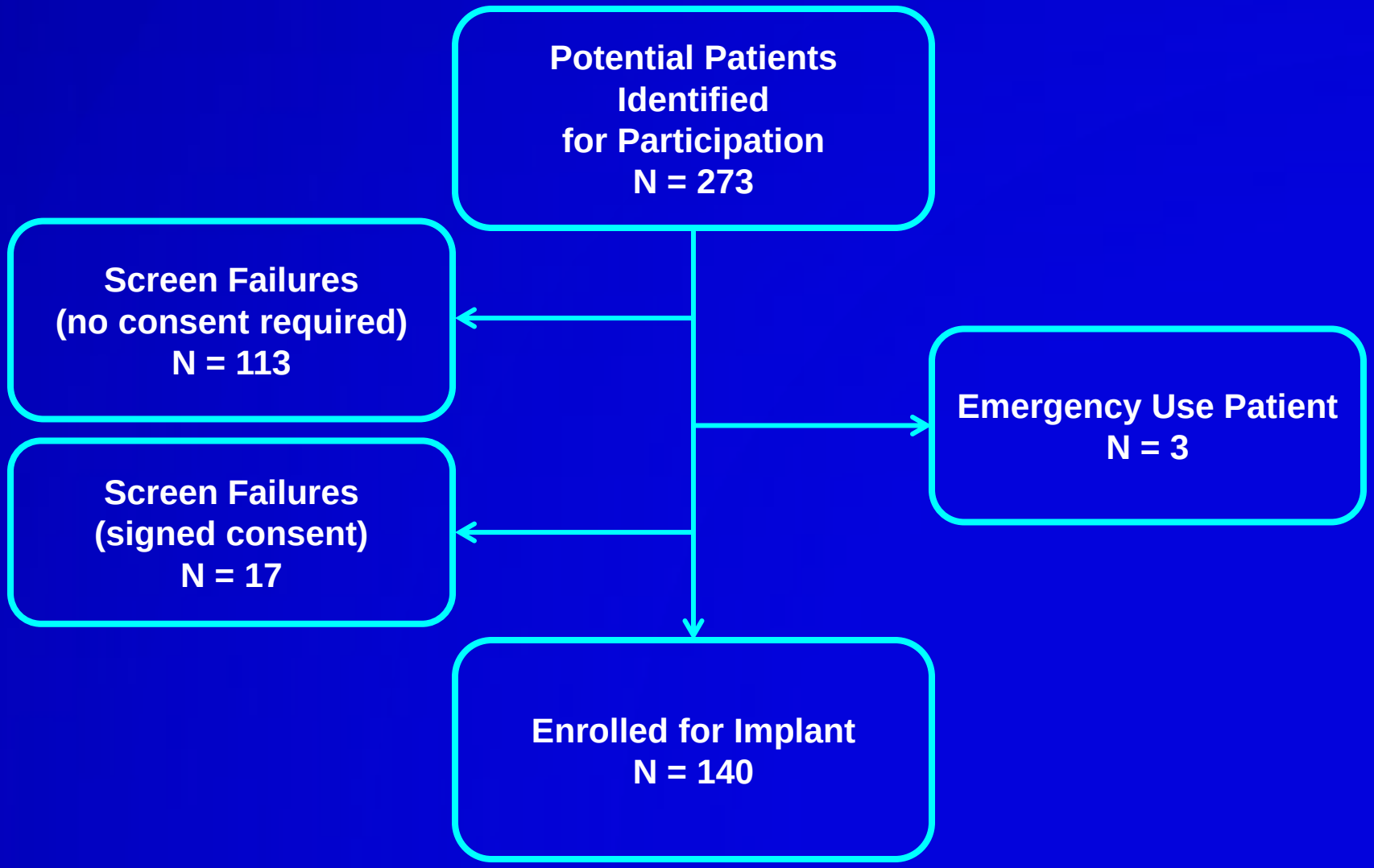
- At FDA request follow-up for status at 6 months post screen failure was sought
- Patients received another device, transplant or no treatment

			Died
HeartMate II	12/17	(71%)	1/12
Abiomed	1/17	(6%)	1/1
Transplant	2/17	(12%)	0/2
None	2/17	(12%)	0/2

Enrollment of Women

- From UNOS as of January 6, 2012:
  - 3126 pts listed for heart
  - 2301 males – 73.6%
  - 825 females – 26.4%
- Female enrollment in HeartWare trial: 28%
- Greater enrollment in HeartWare trial may be related to smaller size of device.

Patient Disposition for Trial



Enrollment of Women

- The percentage of women enrolled exceeded the percent of women listed by UNOS as awaiting transplant.

	n	%
UNOS – awaiting transplant	**825/3126**	**26**
BTT	**39/140**	**28**
Miller et al	**28/133**	**21**
Pagani et al	**67/214**	**24**

Organ Procurement and Transplantation Network website (Accessed 30 March 2012)
Miller LW, Pagani FD, et al. Use of a Continuous-Flow Device in Patients Awaiting Heart Transplantation. N Engl J Med 2007; 357: 885 - 96.
Pagani FD, Miller LW et al. Extended Mechanical Circulatory Support With a Continuous-Flow Rotary Left Ventricular Assist Device. J Am Coll Cardiol. 2009 Jul 21; 54(4):312-21.

6 Minute Walk: Comparison to Pagani et al. Paper

Subjects included: all patients who walked at both baseline and 6 months (and had a distance (m) reported).

Walked Baseline and 6 Months	Baseline (m)	Month 6 (m)
HeartWare HVAD	260 ± 140 (n=25)	338 ± 202 (n=25)
Pagani et al.	201 ± 140 (n=14)	368 ± 125 (n=14)

Subjects included: all patients who did not walk at baseline (for any reason), but walked at 6 months (and had a distance (m) reported).

Walked at 6 Months but not at Baseline	Month 6 (m)
HeartWare HVAD	333 ± 125 (n=30)
Pagani et al.	326 ± 232 (n=95)

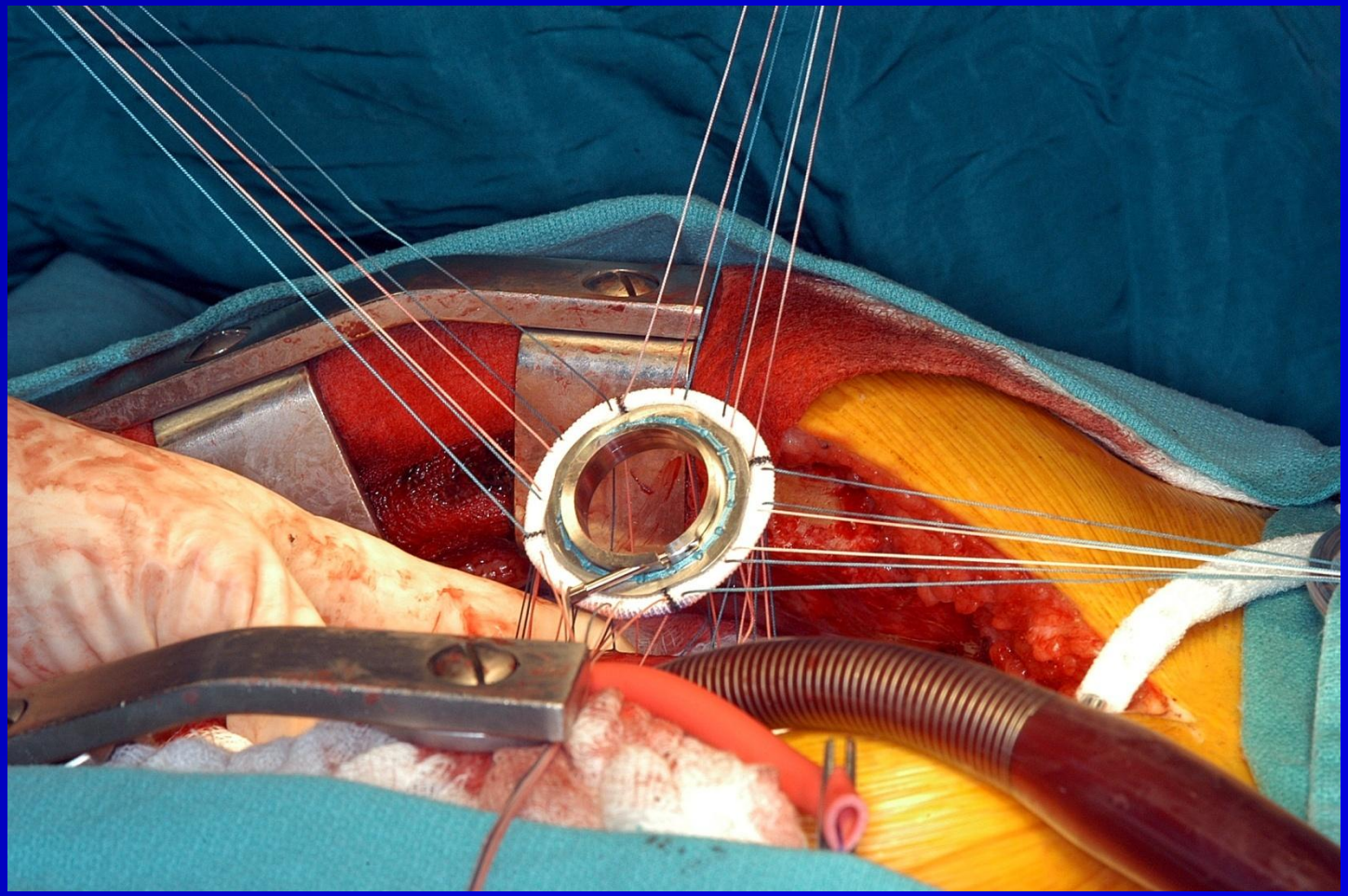
Appendix K Clarification

Patient ID	CEC Serious & Device Related	Description
011-002	2 events	Cardiac tamponade bleed & sepsis/tissue exiting LVAD infection
005-004	-	
002-002	-	
001-005	-	
001-008	1 event	ICVA
003-001	-	
010-002	1 event	ICVA
006-004	-	
017-006	-	
027-010	1 event	Mediastinal bleed
034-005	-	
006-003	1 event	Driveline exit site infection
011-007	-	
006-007	-	

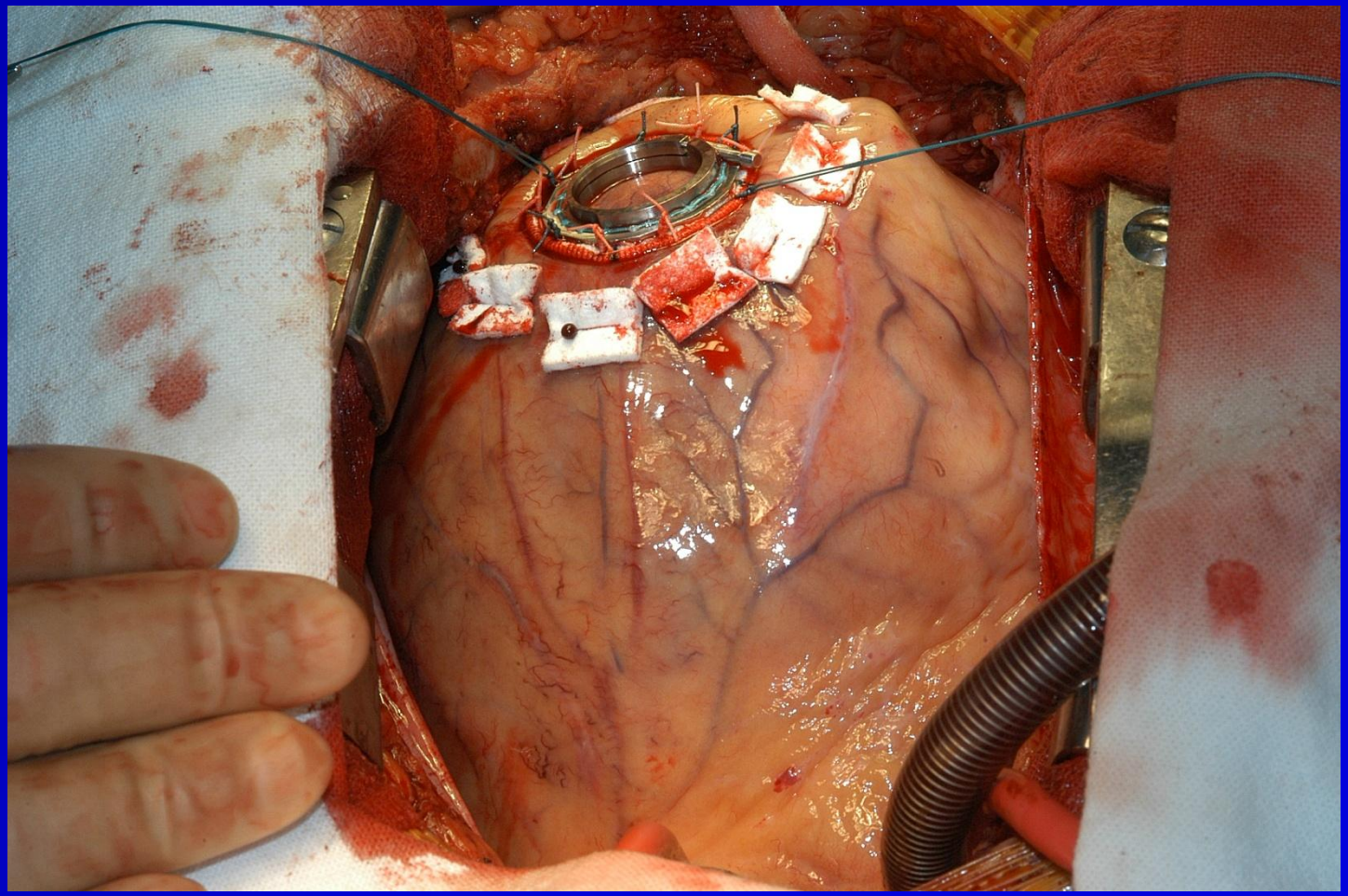
Appendix K Clarification

- Listed are serious AND device related
- Original appendix site reported
- Sites options regarding relatedness
  - Not related – procedure related/patient condition
  - Degrees of Related: unlikely related, possibly related, probably related, related
- CEC doesn’t determine degree of relatedness
  - Just determines relatedness in YES or NO fashion

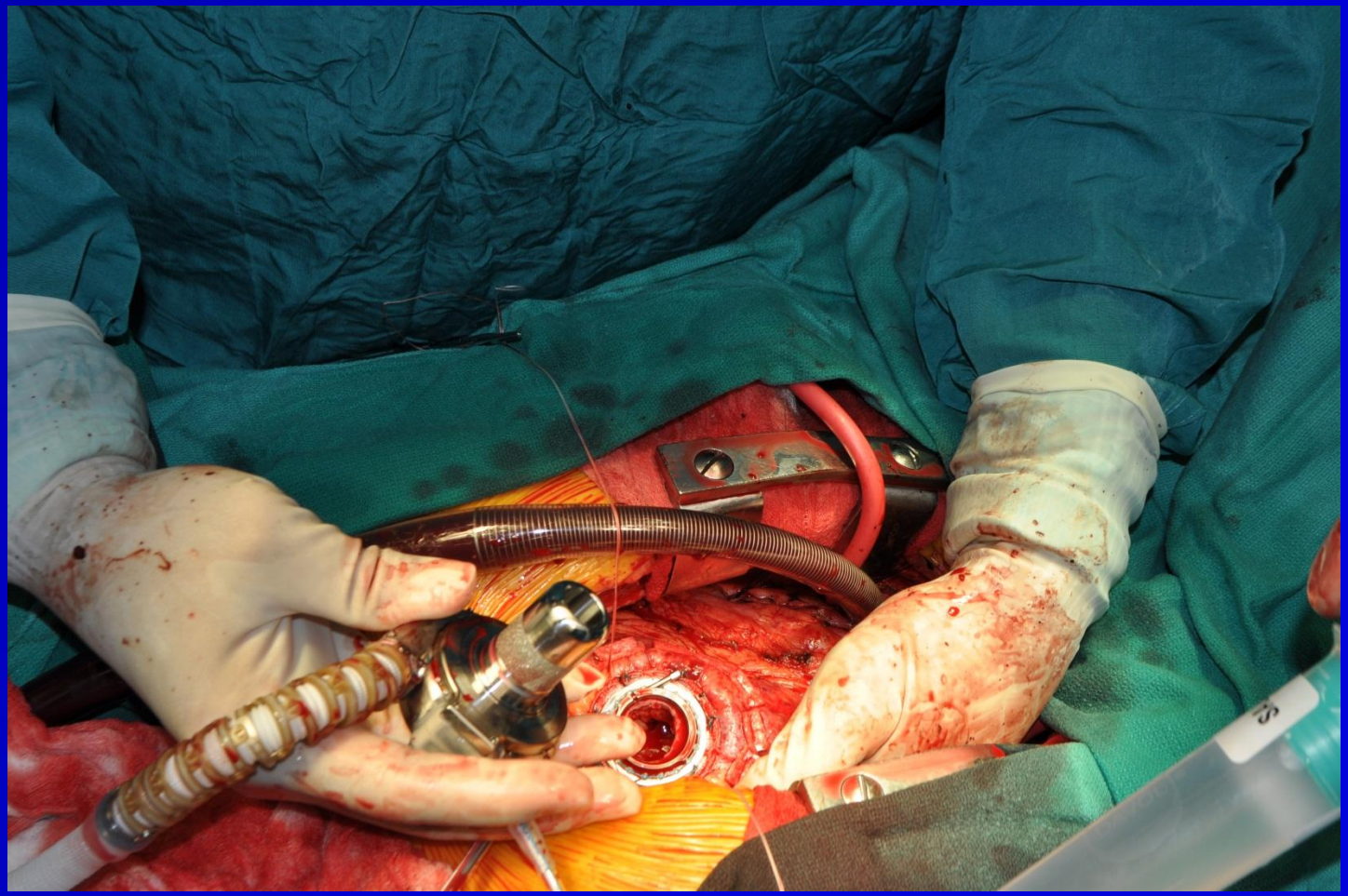
Apical Sewing Ring



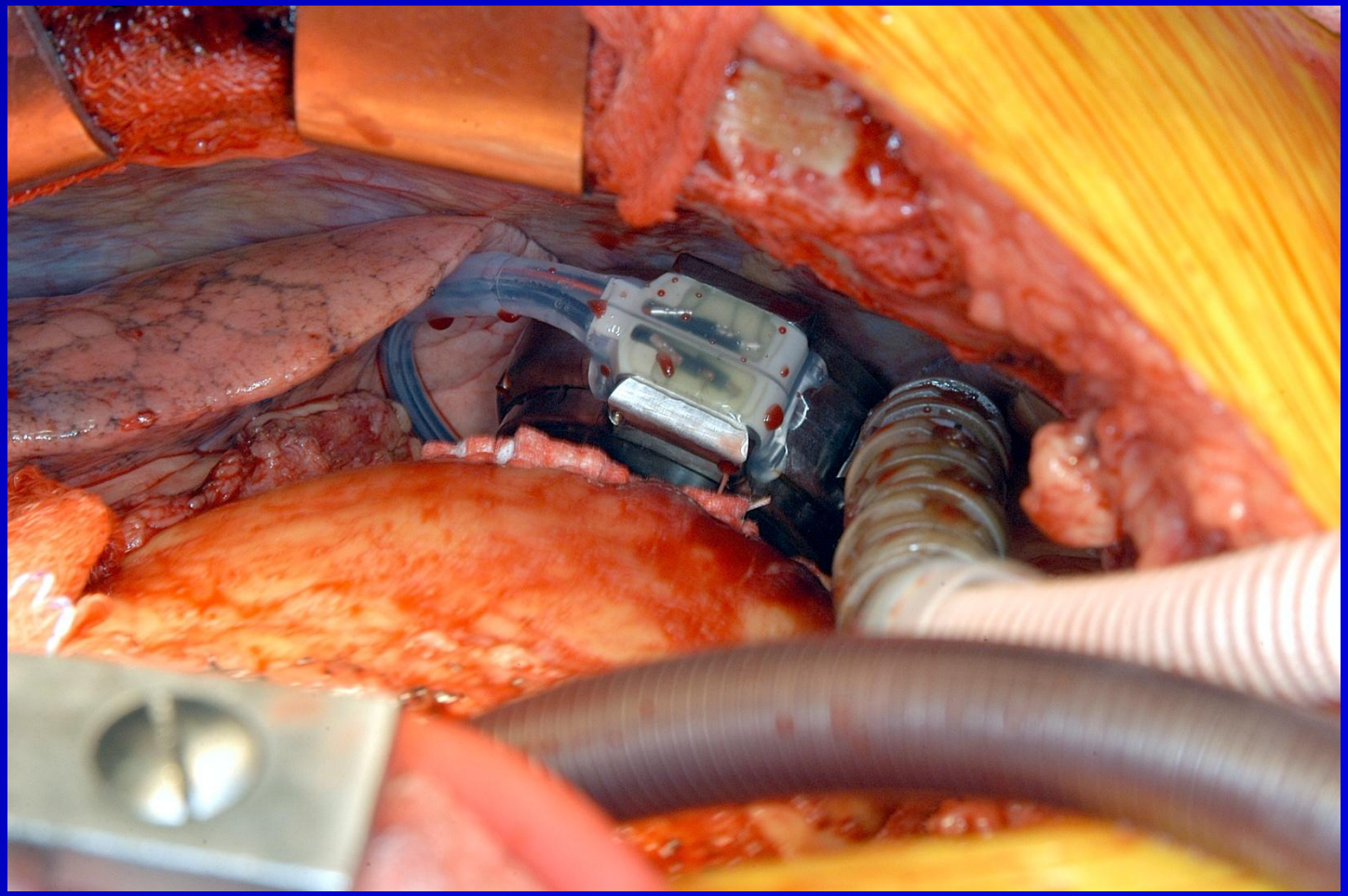
Apical Sewing Ring



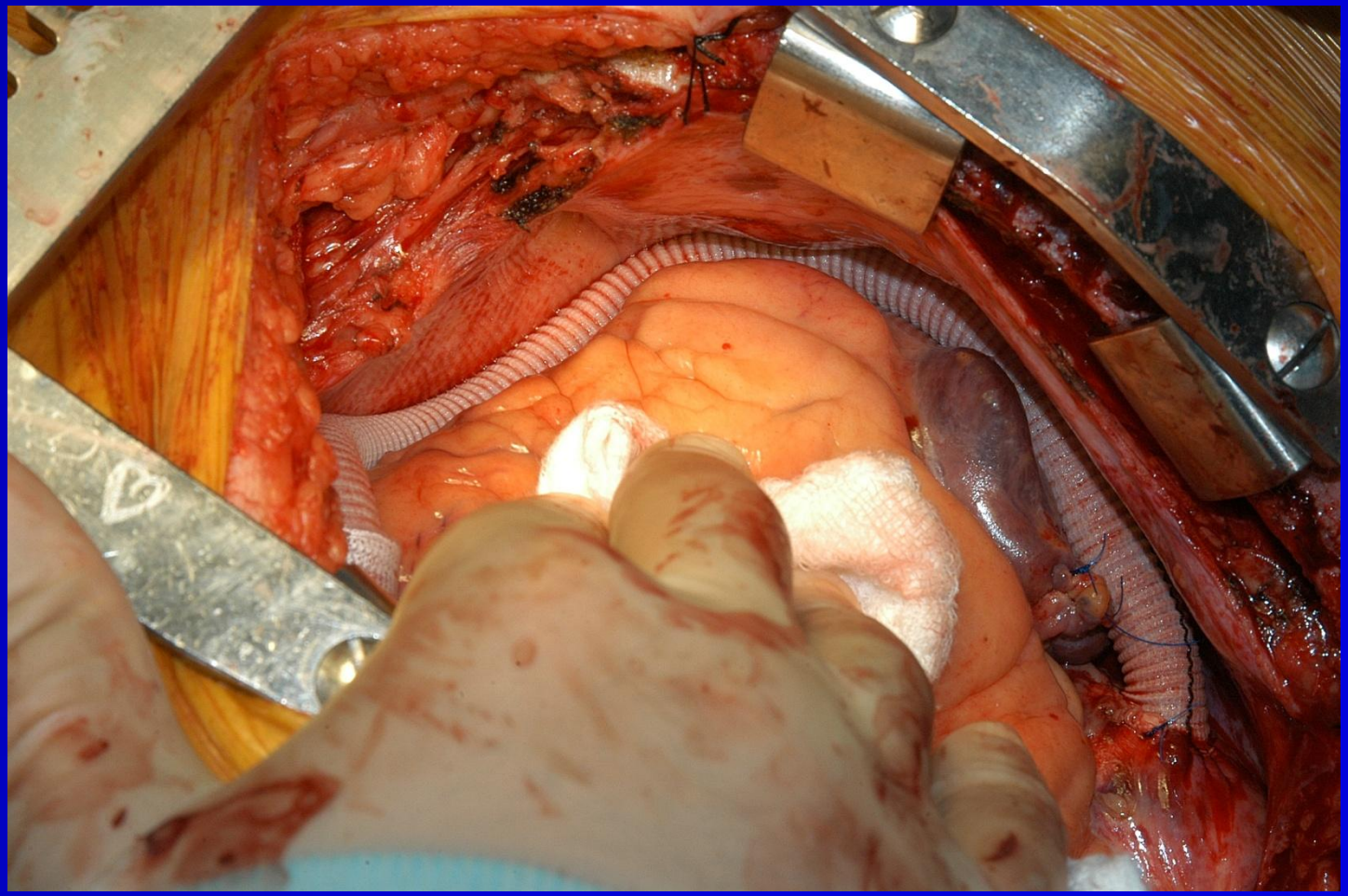
HVAD Insertion



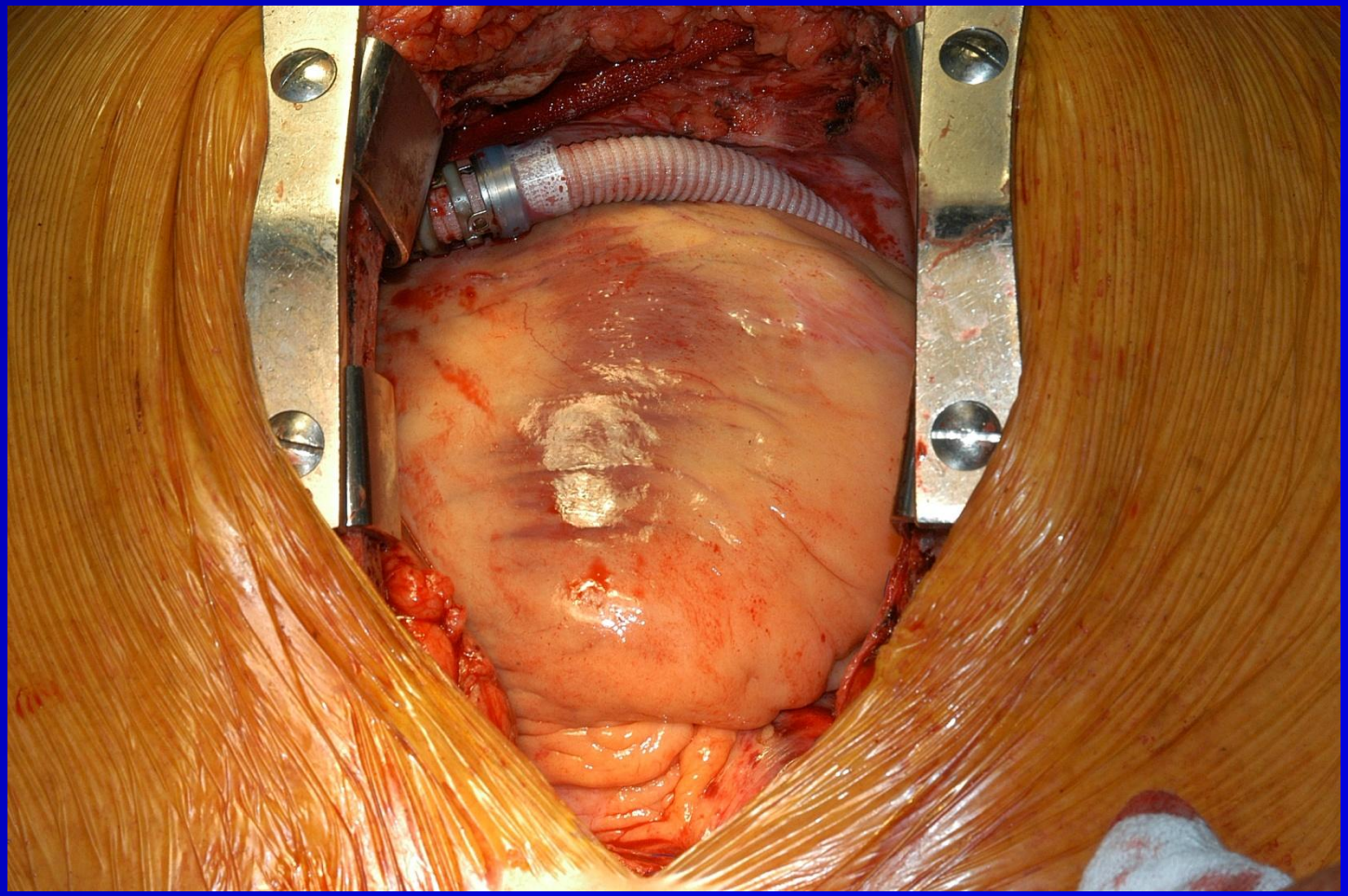
HVAD Implant



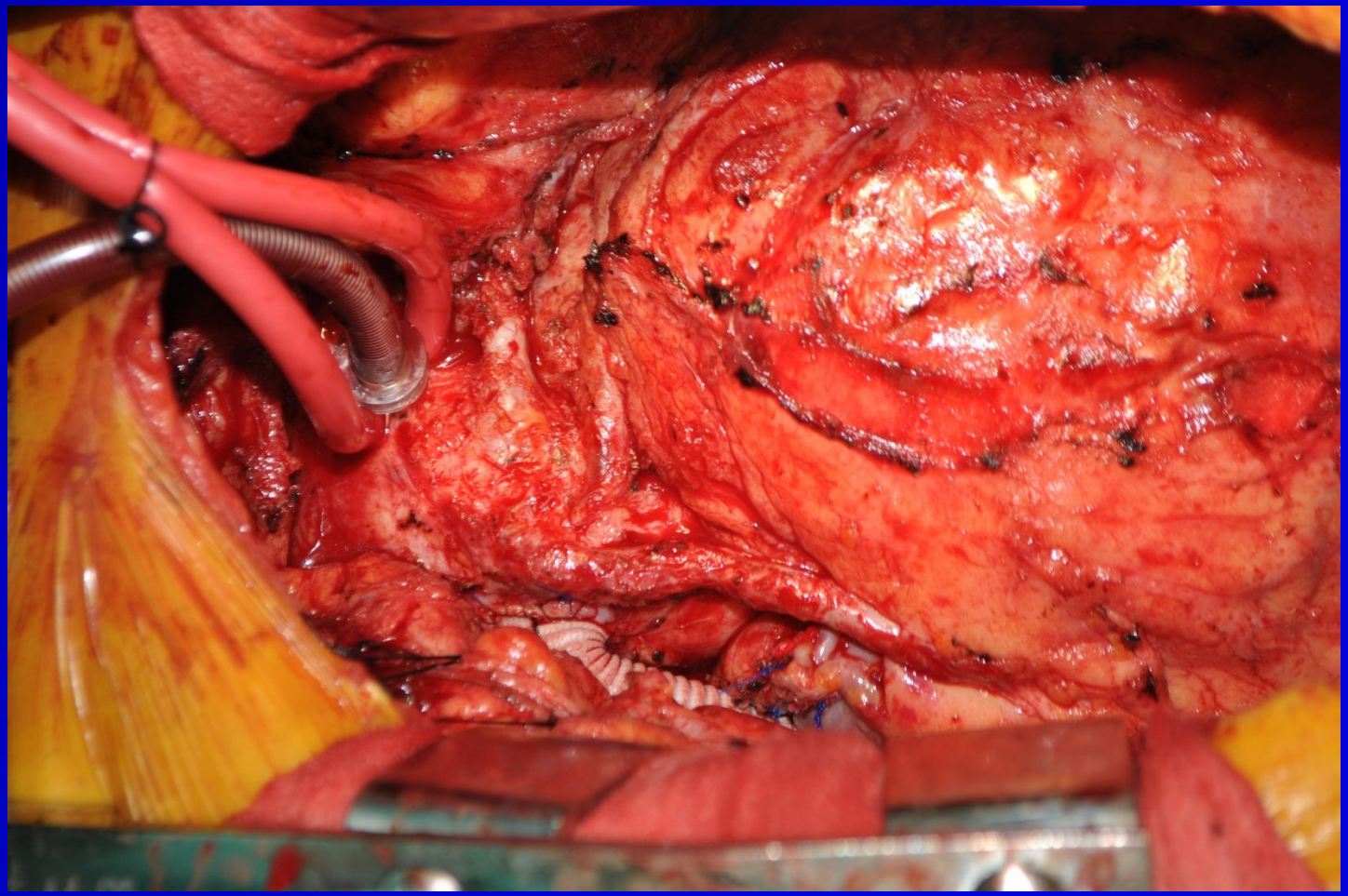
Outflow Graft



Outflow Graft

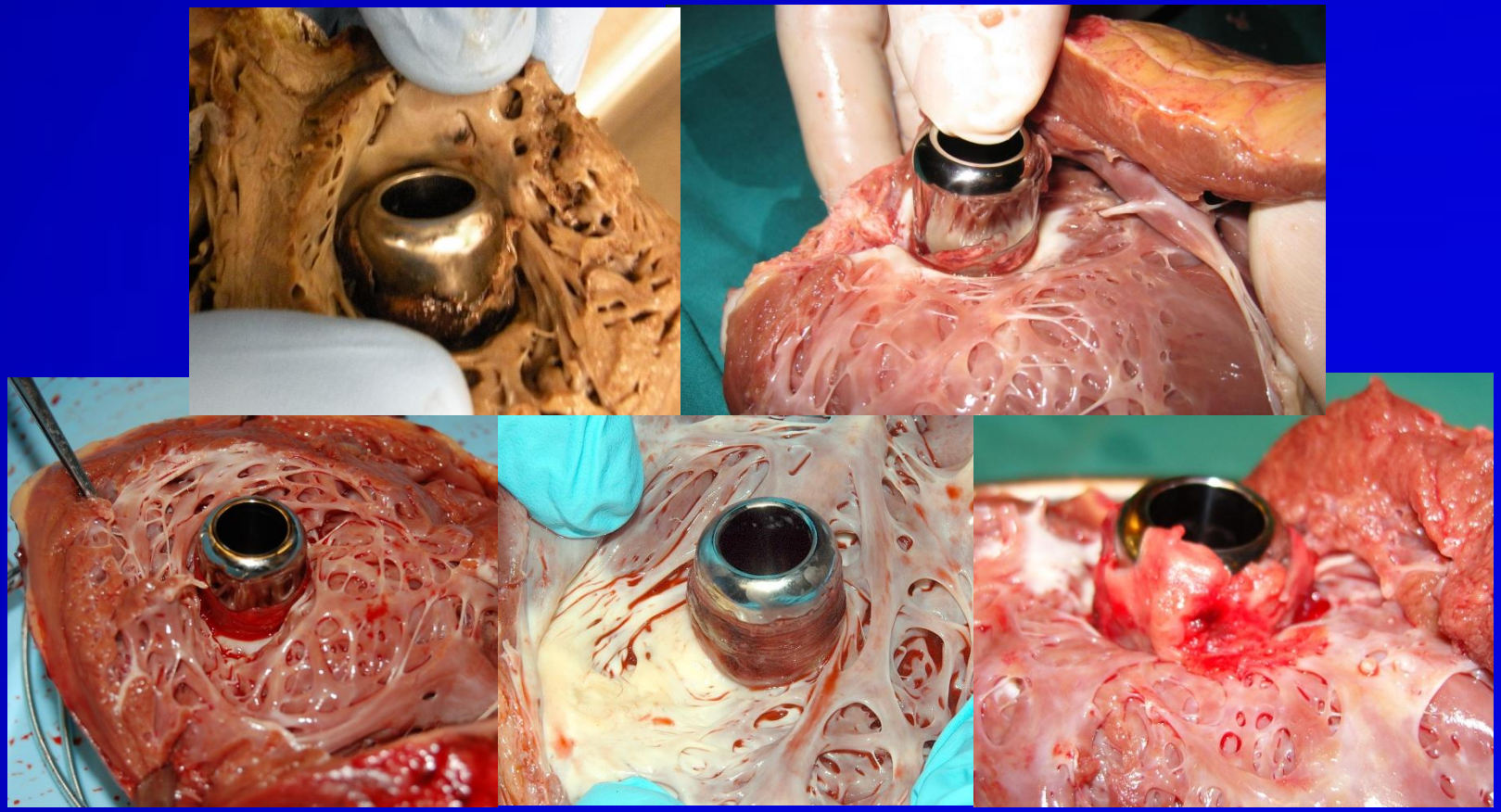


Outflow Graft (limited aortic space)



Sintered Inflow Cannula

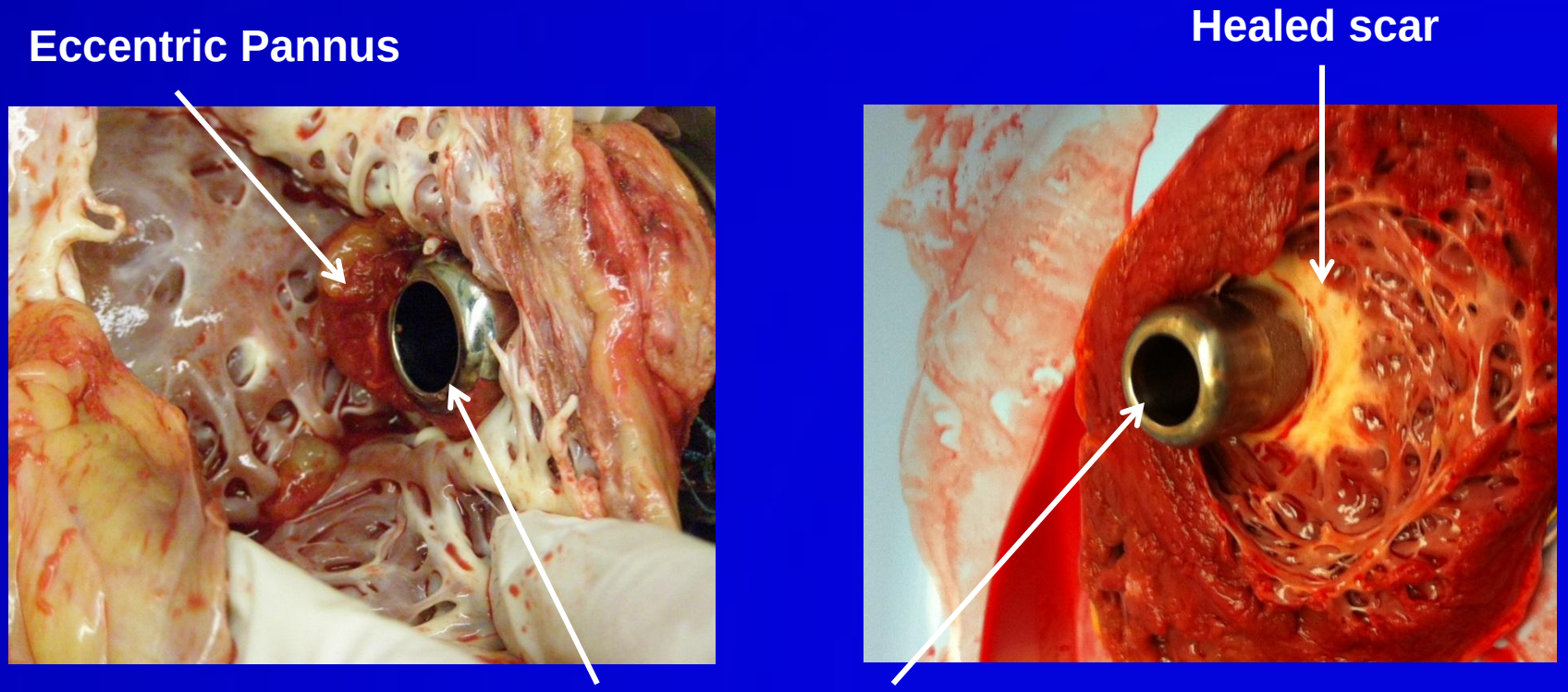
Why Sintering Was Added



Smooth inflow does not enable tissue incorporation and endothelialization

Smooth Inflow: Eccentric Healing Tissue

- Although rare, pannus tissue in the pump inflow has resulted in occlusion and pump replacement



Treatment Emergent Adverse Events – Sintered 0-30 Days Adjudicated (1-2)

	Sintered (N=62)		
INTERMACS Category Adverse Events	Patients	% Patients	# Events
Re-Hospitalization	0	0%	0
Re-Operation	3	4.8%	3
Transfusion: >=4 within 7 Days	5	8.1%	6
Cardiac Arrhythmia	3	4.8%	3
Ventricular	2	3.2%	2
Supraventricular	1	1.6%	1
Device Malfunction/Failure	0	0%	0
Hemolysis	0	0%	0
Hepatic Dysfunction	1	1.6%	1
Infection	3	4.8%	4
Non-Device Related	3	4.8%	4
Sepsis	0	0%	0
Driveline Exit Site	0	0%	0

Treatment Emergent Adverse Events – Sintered 0-30 Days Adjudicated (2-2)

	Sintered (N=62)		
INTERMACS Category Adverse Events	Patients	% Patients	# Events
Ischemic CVA	0	0%	0
Hemorrhagic CVA*	2	3.2%	2
TIA	0	0%	0
Psychiatric	1	1.6%	1
Renal Dysfunction	0	0%	0
Respiratory Dysfunction	3	4.8%	3
Right Heart Failure Inotropic Therapy	5	8.1%	5
RVAD	2	3.2%	2
Venous Thromboembolism	1	1.6%	1
UADE	0	0%	0
Other	10	16.1%	13

1 Sintered Exchange to date non-thrombus

*Pending adjudication

Performance Goal Assessment: Females

- 29 out of 39 females succeeded (74.4%)
- 10 Failures
  - 4 Patients alive on original device not 1A/1B
    - 3 UNOS status 7
    - 1 UNOS status 2
  - 3 Exchanges
    - 2 Thrombus
    - 1 Right Heart Failure exchanged to a BiVAD
  - 3 Deaths